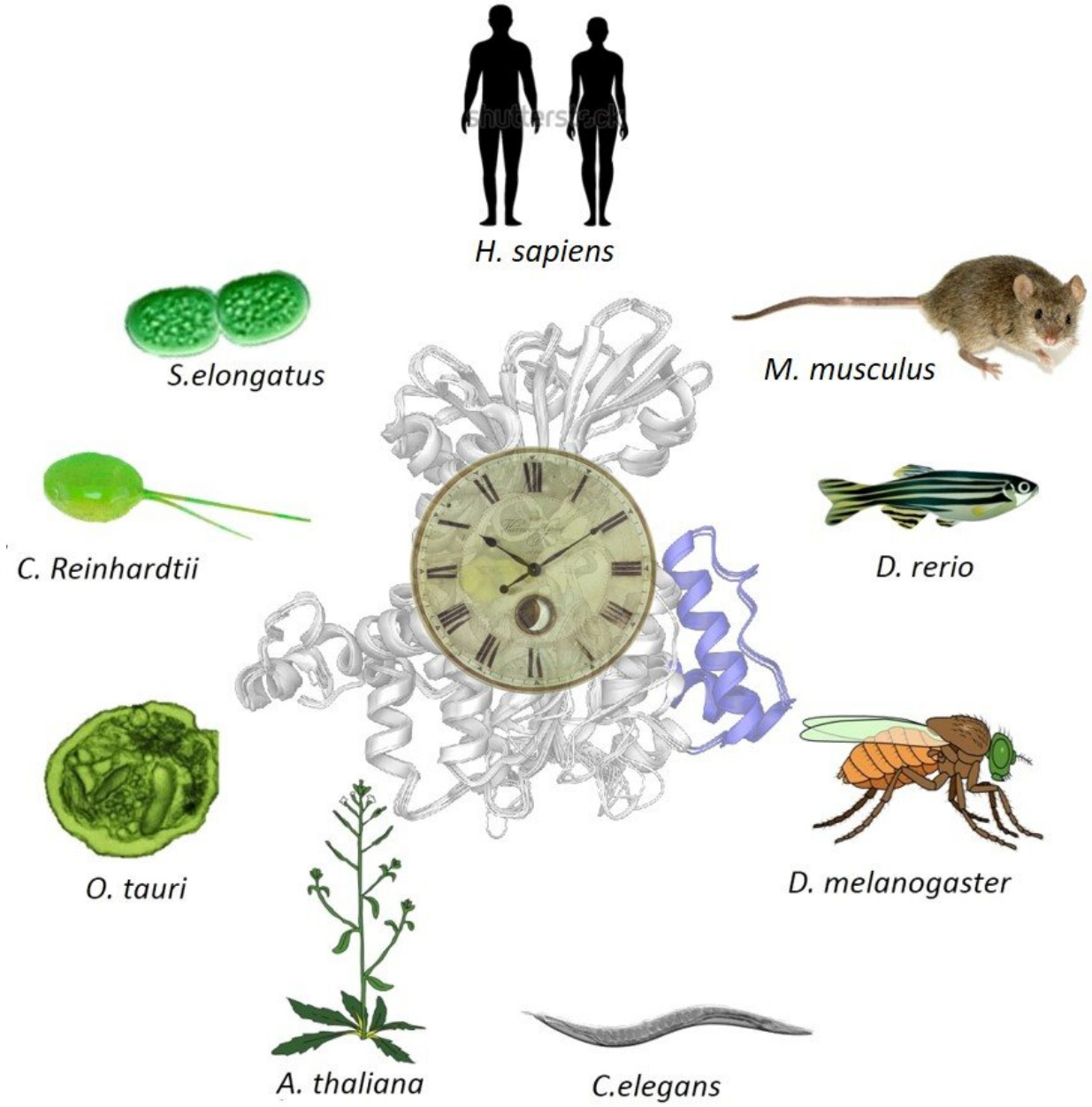
From bacteria to you: The biological reactions that sustain our rhythms

June 12 2020



Biological methylation and the body clock are conserved during 2.5 billion years of evolution, to the extend that reprogramming the mammalian methyl cycle using a bacteial enzyme prevents methylation deficiencies is viable. Credit: Kyoto University/Jean-Michel Fustin

Every second of every day, countless biochemical reactions take place in our bodies' cells. The organization of this complex system is the result of billions of years of evolution, fine-tuning our functions since the first primordial organisms.

One such vital reaction is "methylation," where a methyl group—a carbon atom linked to three hydrogen atoms—attaches itself to a target molecule. Methylation is involved in the regulation of everything from DNA to proteins, and it is so vital that it can be found in all living organisms.

In a recent paper published in *Communications Biology*, a team of researchers lead by Jean-Michel Fustin and Hitoshi Okamura from Kyoto University's Graduate School of Pharmaceutical Sciences has uncovered an intimate connection between methylation and the body's circadian rhythms: a link that exists even in organisms that don't traditionally "sleep," such as bacteria.

"Disfunction in methylation can cause any number of pathologies, from atherosclerosis to cancer," explains Fustin. "Previously we discovered that inhibiting methylation in mice and human cells disrupted their body clocks."

Methylation and the circadian rhythm, he adds, are ancient mechanisms retained in many organisms from bacteria to humans. "So, we

hypothesized that the link between the two was also ancient."

The team began by collecting cells and tissue samples from different organisms and measuring their biological rhythms. On average, all organisms run on periods of 24 hours.

The next step was to find out what happens when methylation is disrupted, and as anticipated, significant alterations in the circadian clock were detected in all cell types, including in plants and algae. However, cyanobacteria—photosynthetic bacteria—seemed relatively resistant.

"The methylation pathway in bacteria is slightly different from other organisms. But when an alternative compound inhibiting a different part of methylation was used, the circadian clock was indeed strongly affected there as well," Fustin continues.

Applying their findings, the team then took a gene that is key in controlling bacterial methylation and introduced it into mouse and human cells. Exceptionally, the bacterial gene was able to protect the cells from the first methylation inhibition compound, with no alterations observed in circadian rhythms.

"Not only did we find the evolutionarily conserved link between two ancient biological pathways—methyl metabolism and biological clocks—but we also opened the door to a possible new treatment for methylation deficiencies," concludes Okamura.

"All organisms are more alike than you might think, and knowledge about how we evolved will allow us to better understand ourselves and the natural world."

More information: Jean-Michel Fustin et al, Methylation deficiency

disrupts biological rhythms from bacteria to humans, *Communications Biology* (2020). DOI: 10.1038/s42003-020-0942-0